DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The disclosure cited is not sufficient to establish that at the time the application was filed that the inventors had position of the negative limitation "carboxymethyl cellulose". It appears that cross-linked carboxymethyl cellulose resulted in tablets that disintegrated within 47 seconds (Specification, page 16, Comp. Example 6-1). As such, there is no showing that all types of cellulose would result in a disintegration time that is not within 47 seconds. Further, the application when filed specifically recited that the composition did not contain microcrystalline cellulose. The Specification as indicated also had comparative examples using the cross-linked carboxymethyl cellulose or low-substituted hydroxypropyl cellulose. Since the inventor did not when it clearly had opportunity to do so to exclude all types of cellulose, there is insufficient evidence that the inventor had contemplated the above limitation at the time the application was filed. See *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) ("If n-propylamine had been used in making the compound instead of n-butylamine, the compound of claim 13 would have resulted. Appellants submit to us, as they did to the board, an imaginary specific example patterned on specific example 6 by which the above butyl compound is made

so that we can see what a simple change would have resulted in a specific supporting disclosure being present in the present specification. The trouble is that there is no such disclosure, easy though it is to imagine it."); *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion").

The Applicant is confusing enablement with lack of written description. Although the Specification does enable one of ordinary skill in the art to prepare a tablet without cellulose or cellulose derivative, the Specification does not describe a negative limitation excluding cellulose or cellulose derivatives as a genus or carboxymethylcellulose. See *Vas-Cath Inc. v. Mahurakar*, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991)(description of specific embodiment does not necessarily provide written description of broadly claimed subject matter or other members falling within a class).

The Applicant cites to the corresponding patent publication as support for the claimed amendment. However, there is nothing is the cited paragraphs which exclude cellulose. Further, Specification, Page, 7, lines 19, 20 states that "[o]ther pharmaceutically acceptable excipients may be also used in the present invention, including but not limited to . . . .". As such, the Specification, contrary to the Applicant's arguments, indicates that the excipients are not limited to those specifically recited. Thus, the Specification does not provide sufficient support for the claimed negative limitation excluding carboxymethylcellulose.

Although the Applicant has amended the claims to exclude only microcrystalline cellulose, low-substituted hydroxypropyl cellulose and carboxymethylcellulose, the claims are still not support by Specification and claims as originally filed. The Specification does not disclose the compound "carboxymethylcellulose". The Specification discloses a comparative test using cross-linked carboxymethylcelulose. Carboxymethyl cellulose and cross-linked carboxymethyl cellulose are not the same compounds; the latter is a disintegrant whereas the former is a binder (See Matoba et al. (US Pat. 5,456,920), Column 9, lines 14-23).

The Applicant cites to an inventor's affidavit (4/12/2007), however, the same only goes to the issue of enablement. There is nothing in said affidavit which shows that the Specification and claims as originally filed described a negative limitation excluding carboxymethylcellulose, much less cellulose or cellulose derivatives.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/78292 in view of Serpelloni et al. (US Pat. 5,573,777).

WO 00/79292 discloses that a quickly disintegrating solid preparation comprising an active ingredient, such as acetaminophen, scopolamine, famotidine or meclizine, D-mannitol with a mean particle diameter of 30 micrometers to 300 micrometers, crospovidone and a cellulose compound, such as crystalline cellulose, powder cellulose, low substituted

hydroxypropyl cellulose and carmellose (Pg. 2, lines 22-24, Pg. 3, lines 10-19, Pg. 5, lines 3-29, Pgs. 6, 7, Pg. 8, lines 1-7;Column 2, lines 24-27, 56-68, Column 3, lines 1-5, Column 4, lines 21-68, Column 5, Column 6, lines 1-18). It is disclosed that the amount of the mannitol is 40 to 95 parts per 100 parts of the solid pharmaceutical preparation and that the amount of crospovidone is preferably 1 to 10 parts per 100 parts of the solid pharmaceutical preparation (Page 10, lines 17-23;Column 7, lines 52-59). It is disclosed that the solid preparation can contain foaming agents, such as sodium bicarbonate, sodium carbonate, sour agents including, citric, tartaric or malic acid, sweeteners, such as aspartame, saccharin, lubricants, such as magnesium stearate, and flavoring agents, in amounts generally used in the preparation of pharmaceutical preparations provided that they do not interfere with the effect of the invention (Page 11, lines 20-29, Page 12, lines 1-19; Column 8, lines 31-68). It is disclosed that the time required for intraoral disintegration is preferably about 5 to about 60 seconds and that the tablet hardness is preferably about 10 to 150 N, and, thus, can be used by patients, aged people and children who have difficulty swallowing medicine and is excellent in long-term storage and stability (Pg. 14, lines 1-21;Column 10, lines 8-43). The cites to column and line numbers refer to US Patent 6,740,339 which is the 371 of WO 00/79292.

Serpelloni et al. discloses mannitol which is prepared by atomizing an aqueous solution of mannitol and granulating the atomized powder where the mannitol has a mean diameter of 135 microns with approximately 86% of the particles having a size greater than 100 microns, moderate and not excessive friability, good ability to flow, a very high rate of solubilization of 26 seconds and forms tablets having a hardness of 78 N (Column 10, lines 1-49, Column 12, lines 40-63).

The prior art discloses a tablet that disintegrates within 5 to 60 seconds, containing mannitol, crospovidone, and one or more organic acids, foaming agents, sweeting agents, diluents, and flavoring agents. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the use of spray-dried mannitol of which at least 80% has an average particle size over 100 micrometers in combination with crospovidone. However, the prior art amply suggests the same as the prior discloses the use of mannitol in combination with crospovidone in a tablet that disintegrates in less than 60 seconds and discloses a mannitol having properties which fall within the scope of the claimed mannitol. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the Serpelloni et al. mannitol would be suitable for use in the WO 00/78292 product and that the product would be suitable for persons who have difficulty in swallowing solid medications.

The Examiner reinstates the rejection herein as the claims only exclude microcrystalline cellulose, low-substituted hydroxypropyl cellulose and carboxymethyl cellulose. The prior art does not require the use of microcrystalline cellulose, low-substituted hydroxypropylcellulose or carboxymethylcellulose.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chauveau et al. (US Pat. 6,106,861) in view of Serpelloni et al. (US Pat. 5,573,777) and Wehling et al. (US Pat. 5,178,878).

Chauveau et al. disclose tablet which disintegrates in less than 40 seconds which overcomes the drawback of prior art tablets having a gritty and pasty sensation on ingestion containing a coated active ingredient, such as paracetamol, a soluble diluent which is a directly compressible product having an average particle diameter of between 100 and 500 micrometers, including mannitol, a disintegration agents, such as crospovidone or cross-linked sodium carboxymethylcellulose, where the respective proportions of disintegration agent and soluble diluent is from 3 to 15%, preferably 5 to 10%, by weight and 40 to 90%, preferably 50 to 70%, by weight, respectively, based on the weight of the tablet, sweetener, flavouring and lubricant which is prepared by compression of a mixture of the same with sufficient force for it to be handled and packaged industrially, then carried and handled by the patient without any particular precautions (See Columns 1-3, Column 4, lines 1-10). Tablets are disclosed containing coated active ingredient, mannitol for direct compression (36.7%, 56.6%, 63.3%, 38%, 52.5%) crystalline powder mannitol, crospovidone (8.6%, 5%, 5%, 8.6%,10%), sweetener, flavoring and magnesium stearate which disintegrate in less than 40 seconds which are prepared by mixing the components and compressing into tablets (Column 4, lines 11-68, Columns 5-6, Column 7, lines 1-14).

Serpelloni et al. is cited for the same reasons as above and is incorporated herein to avoid repetition.

Wehling et al. disclose an effervescent tablet which as a dissolution time of less than about 1 minute contatining mannitol (225 mg), sweetener, flavoring, magnesium stearate, silicon dioxide, sodium bicarbonate, citric acid and microparticles of an active ingredient (Colum 13, lines 1-15). It is disclosed that the dosage form can include non-effervescent disintegrants (Column 7, lines 29-34). It is disclosed that intrinsic lubricants can materially retard

disintegration of non-effervescent tablets, however, that the incorporation of the effervescent disintegration agents overcome any such retardation (Column 9, lines 20-25). It is disclosed that the tablet should contain an amount of effervescent disintegration agent effective to aid in the rapid and complete disintegration of tablet when orally administered, i.e. the tablet should dissolve in the mouth in between about 30 seconds and 5 minutes (Column 6, lines 49-56). It is disclosed that the effervescent agents include the combination of a soluble acid source, such as citric, tartaric, fumaric or malic acid and an alkali metal carbonate or carbonate source, such as calcium carbonate, sodium bicarbonate or potassium bicarbonate (Column 5, lines 56-68, Column 6, lines 1-18).

The prior art discloses a tablet that disintegrates within 40 seconds, containing a coated active ingredient, a direct compression mannitol, crospovidone, sweetening agents, diluents, and flavoring agents. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the use of spray-dried mannitol of which at least 80% has an average particle size over 100 micrometers in combination with crospovidone or the use of an effervescent agent and/or organic acid. However, the prior art amply suggests the same as the prior discloses the use of a direct compression mannitol having an average particle size from 100 to 500 micrometers in combination with crospovidone in a tablet that disintegrates in less than 40 seconds and discloses a spray dried mannitol having a mean average diameter of 135 microns which can be compressed into tablets and rapidly disintegrating tablets containing effervescent agents, including combinations of organic acids and alkali metal carbonate and bicarbonates. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the Serpelloni et al. mannitol would be suitable for use in the Chaveau et al. and that the product would not leave a

gritty or pasty sensation and have sufficient hardness to withstand packaging and handling and that the addition of an organic acid and alkali metal carbonate or bicarbonate would provide effervescence which would expect to overcome any possible retardation of disintegration due to the presence of lubricants in the tablet.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
April 11, 2008

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616